




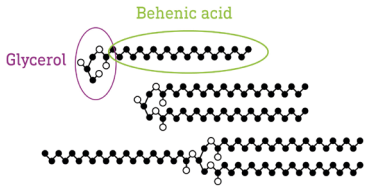
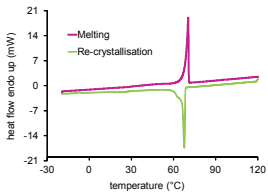
Compritol[®] 888 ATO

A smart solution to sustain drug release



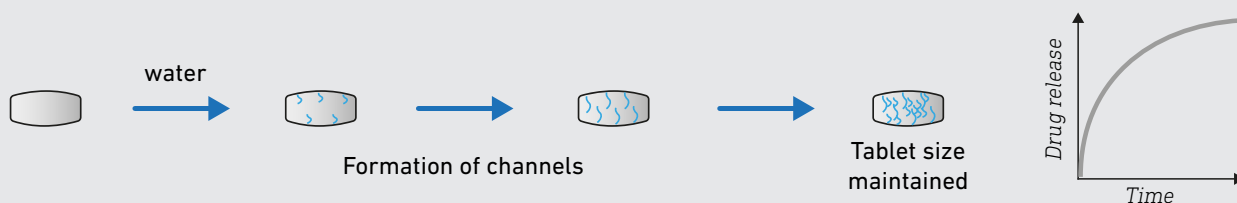
Advantages of Compritol® 888 ATO in sustained drug release

- Predictability and reproducibility of drug release
- Good *in vitro in vivo* correlation
- Robustness of lipid-based sustained release (SR) matrices in physiological conditions
- Process flexibility

Compritol® 888 ATO properties		Advantage in SR matrix
Insoluble in aqueous solution		Lipid matrix does not swell, dissolve or erode, irrespective of the media: water, 0.1N HCl, pH 4.5 buffer and 40% ethanol solution
Non digestible		Robustness in physiological conditions: no impact of enzymes or bile salts
Insoluble in hydro-alcoholic media		Reduced risk of dose dumping
Non-ionic and chemically inert		Compatible with APIs and excipients
High melting point, narrow melting range and rapid recrystallization behavior		Ideal for cold (direct compression, wet granulation) and hot processes (melt extrusion, melt granulation, solid dispersion...)

Predictability and reproducibility of drug release

Compritol® 888 ATO is a water-insoluble excipient: it does not swell or erode in contact with the aqueous medium. When used as an SR agent in tablet, it forms an inert matrix through which the drug diffuses out slowly. The matrix geometry/tablet size does not change throughout dissolution. Therefore, it is suggested that drug release is governed by pure diffusion and the release kinetic is principally first order.



Single matrix: SR tablet with Compritol® 888 ATO

Straightforward development

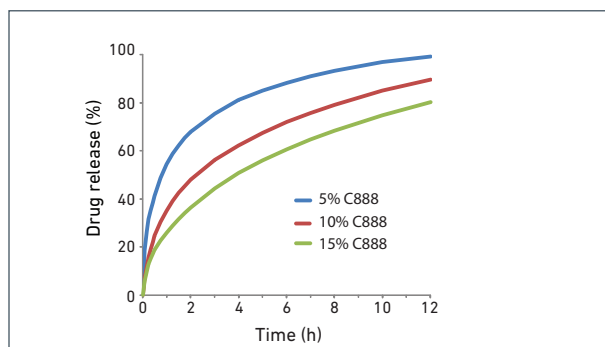
Starting point

The Active Pharmaceutical Ingredient (API) aqueous solubility determines the concentration of Compritol® 888 ATO and the type of diluent to use:

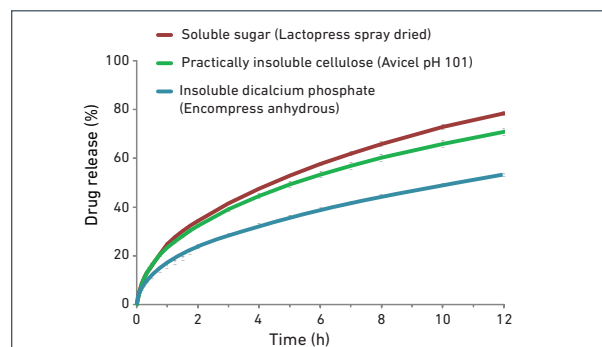
- The higher the drug aqueous solubility, the higher the Compritol® 888 ATO concentration
- Water soluble diluents speed-up drug release

API solubility in release medium	<1 mg/mL	1-50 mg/mL	>50 mg/mL
Compritol® 888 ATO concentration	<15%	10-25%	>20%
Diluents type	Water soluble	Soluble and / or insoluble	Water insoluble

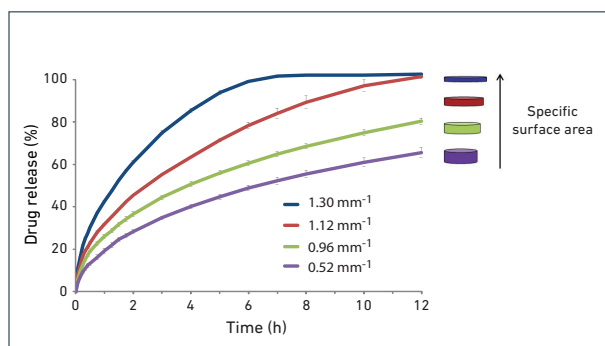
Adjusting the drug release profile



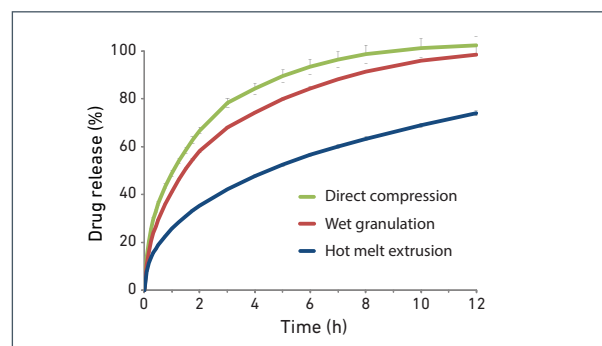
Increasing the concentration of Compritol® 888 ATO decreases the drug release rate.



Decreasing diluent solubility decreases the drug release.



The lower the specific surface area, the slower the drug release.



Switching from a cold to a hot process decreases the drug release.

Ask for our complete formulation guideline, with case studies, trouble-shooting tips and much more

Dual matrix: SR tablet with Compritol® 888 ATO and HPMC

Reduce the SR agent concentration

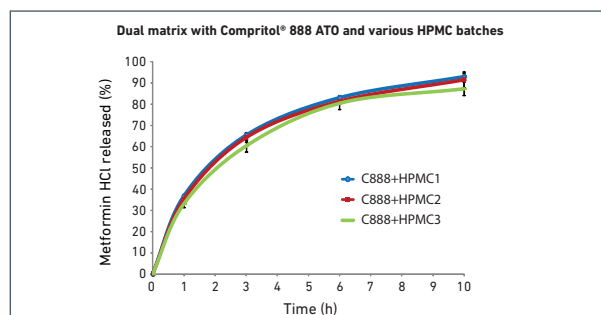
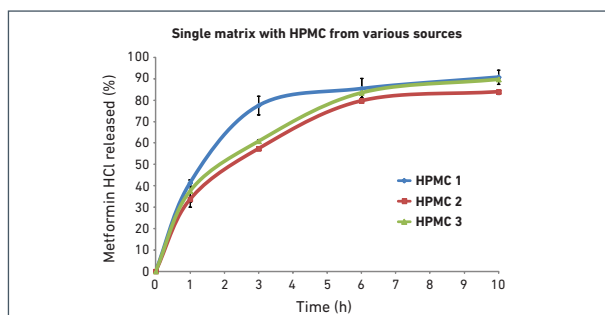
In single matrix, HPMC is frequently used at 30% to achieve sustained release. In a dual matrix, the ideal ratio is about 10% Compritol® 888 ATO and 15% HPMC.

Reduce the alcohol quantity used in wet granulation process

In single HPMC matrix, 50% alcohol solution is necessary in wet granulation to prevent sticking. In a dual matrix, 20% alcohol is sufficient.

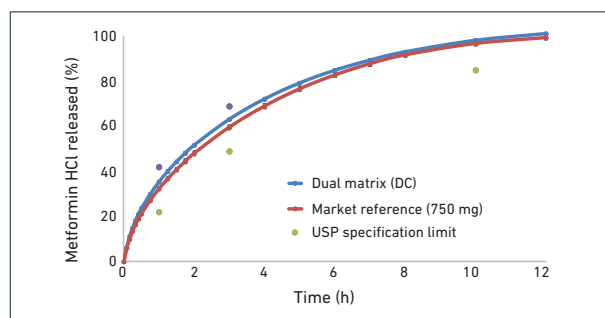
Reduce drug release variability

Addition of Compritol® 888 ATO reduces the inter-batch variability which can be observed with HPMC.



Achieve high drug dose tablet by direct compression

High drug loading was achieved with a dual matrix Compritol® 888 ATO:HPMC in a direct compression process. The dissolution profile was comparable to a market reference (single HPMC matrix, wet granulation + direct compression).



Ask for our case studies with metformin HCl

Develop SR formulations faster with technical support from Gattefossé

To help you develop SR formulations with Compritol® 888 ATO, Gattefossé provides

- ▶ Formulations with model drugs
- ▶ Complete formulation guidelines
- ▶ Case studies
- ▶ Generic drug dossiers



The experts of our Technical Centers of Excellence in France, India, China and USA are at your service to provide technical support and formulation feasibility assessment.

Compritol® 888 ATO at a glance

Definition	Glycerol dibehenate EP Glyceryl dibehenate NF Glyceryl behenate ChP
Regulatory	US DMF (Type IV – Excipient): N°4663 Conformity to EP, USP/NF and Chinese Pharmacopoeia GRAS status (Generally Recognized As Safe)
Production	Obtained by esterification of glycerol with behenic acid, followed by atomization. Reaction process does not involve any catalyst or solvent, ensuring low impurities.
Composition	Well-defined excipient composed of mono-, di- and triglycerides of behenic acid (C ₂₂), the diester fraction being predominant (40-60%).
Physicochemical properties	Fine white powder, mean particle diameter 50 µm Melting point 71°C and rapid recrystallization
Precedence of use	<p>Glyceryl dibehenate (UNII: R8WTH25YS2) is listed in the FDA Inactive Ingredient Database for sustained, delayed and controlled release tablets.</p> <p>Detailed information is available in our Regulatory Datasheet: https://www.gattefosse.com/fr/compritol-888-ato</p> <p>Glyceryl dibehenate is used in sustained release tablets with the following APIs: <i>azithromycin, diltiazem, felodipin, gabapentin, glicazide, guanfacine, ibuprofen, metformin hydrochloride, hydrocosone bitartrate, methylxanthine, metoprolol, molsidomine, nicotinic acid, nisoldipine, paroxetine hydrochloride, prazosin hydrochloride, prednisone, ropinirole hydrochloride, theophylline, tilidine, tramadol, valproic acid and zileuton</i></p>

Quality-by-Design

Gattefossé's state of the art production process ensures high product reproducibility.

Critical Material Attributes such as product composition, particle size and melting point and their impact on tablet properties have been evaluated.

[Ask for our QbD dossier](#)

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COMPRITOL® 888 ATO-6E-69 (3123B5R)

People make our name